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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/019,816	03/27/2002	Michael Valentine Agrez	ADAM-046XX	9944

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EXAMINER	
CANELLA, KAREN A	
ART UNIT	PAPER NUMBER
1643	
MAIL DATE	DELIVERY MODE
04/15/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/019,816	AGREZ ET AL.	
	Examiner	Art Unit	
	Karen A. Canella	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *217-219,221,225,238,244,272,275 and 277* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *217-219,221,225,238,272,275 and 277* is/are rejected.

7)☐ Claim(s) *244* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Clams 217-219, 272 and 277 have been amended. Claims 266, 267, 269 and 278 have been canceled. Claims 217-219, 221, 225, 238, 244, 272, 275 and 277 are pending and under consideration..

Applicant has amended claim 217 to incorporate the limitation that an amino acid linker sequence links opposite end regions of the binding domain. Said limitation is supported by the originally filed disclosure on page 47, line 16 to page 48, line 8.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 217-219, 221, 225, 238, 272, 275 and 277 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The instant method claims are reliant on a genus of modified amino acid sequences, wherein said modified amino acid sequences have greater than 60% homology with the ERK2-binding domains of integrin beta chains 3, 5 or 6, and wherein said modified amino acid sequences bind to ERK2. The specification discloses the reduction to practice of only a single peptide from each of the integrin beta chains of 3, 5 and 6 (page 92, Example 10). Neither the specification nor the art provides teaches as to the 40% of amino acids of the ERK2 binding region of the beta chain of integrins 3, 5 and 6 which can be substituted and still provide a polypeptide which retains the ability to bind ERK2. It is noted that conservation of structure is not necessarily related to conservation of function, and in the instant case, there is no disclosed correlation between structure and function. There is no general knowledge in the art about the relationship between the ability of a polypeptide to bind to ERK2 and the inhibition

of tumor growth. Accordingly one of skill in the art would not accept the disclosure of the ERK2 binding domains of the integrin beta chains 3, 5 and 6 as representative of a modified amino acid sequence having 60% amino acid identity having the ability to bind ERK2 and inhibit the growth of a cancer cell.

Claims 217-219, 221, 225, 238, 272, 275 and 277 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for inhibiting the growth of cancer cells in comprising the administration of ERKs binding domains of the integrin beta chains 3, 5 or 6, does not reasonably provide enablement for a method of inhibiting the growth of cancer cells in vivo or in vitro comprising administering a modified amino acid sequence having greater than 60% amino acid sequence identity with said binding domain and which binds to ERK2. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims..

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is undue include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. In re wands, 858 F.2d 731, 737.8 USPQ2d 1400, 1404 (Fed. Cir. 1988).
(C)As drawn to modified polypeptides .

Claims are drawn to methods reliant on the identity of a modified amino acid sequence having at least 60% overall identity with the binding domain of β3, β5 or β6, wherein said modified polypeptide bind to ERK2. The specification teaches peptides which comprise the integrin-map kinase binding domain and the peptides of SEQ ID NO:2, 3, 22 and 23. The specification fails to teach any structural correlation between retaining or varying the integrin binding domain sequence and the effect on the binding to any ERK2. The art recognizes that the binding of two proteins is influenced by the three dimensional conformation of each of the proteins. Variation of the primary amino acid sequence can have unforeseen consequences on a three dimensional protein structure because the three dimensional structure is governed by

numerous interacting forces (Ibragimova and Eade, Biophysical Journal, Oct 1999, Vol. 77, pp. 2191-2198, cited in a previous action, see page 2191, first column, lines 12-17 and second column, lines 3-8). It is concluded that the art is unreliable for predicting the outcome of amino acid alterations on the three dimensional structure of a protein, and therefore the activity of said protein. It is noted that in order to practice the instant invention to the full scope of the claims it would be necessary to make a modified amino acid sequence having 60% identity to β3, β5 or β6, wherein said amino acid sequence would function as claimed in a method of treating cancer. The specification provides no objective evidence that such a variant can be made an retain the ability to interrupt signaling from β3, β5 or β6, thus there is no reasonable expectation of success that such modified amino acid sequences commensurate with the scope of the claims could be made and used in the claimed invention.

Given the lack of teachings in the specification regarding methods reliant on MAP kinases beyond those or EKR2 and JNK, and the lack of teachings in the specification regarding the making of the required sufficiently homologous polypeptides, one of skill in the art would be subject to undue experimentation in order to practice the broadly claimed methods.

Applicant argues that one of skill in the art would know that conservative substitutions would not substantially modify the structural activity of the original polypeptide and thus would be expected to bind to ERK2. This has been considered but not found persuasive. Firstly, given the teachings of Ibragimova and Eade cited in the previous Office action, there is no reasonable expectation that a polypeptide which has been modified by 40% would function as required, even if the modification were all limited to conservative substitutions. Secondly, the limitation of conservative substitution is not a claim limitation, and thus the broadest interpretation of the claim encompasses non-conservative substitutions as well.

Claim 244 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

All other rejections and objections as set fort or maintained in the previous Office action are withdrawn.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen A. Canella whose telephone number is (571)272-0828. The examiner can normally be reached on 10-6:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on (571)272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Karen A Canella/
Primary Examiner, Art Unit 1643